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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/786,982 | 02/27/2002 | Arjan Scheepens | 37522-10006 | 8750 |

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| EXAMINER | |
|---|---|
| GUCKER, STEPHEN | |
| ART UNIT | PAPER NUMBER |
| 1649 | |

DATE MAILED: 07/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/786,982 | SCHEEPENS ET AL. | |
| | Examiner | Art Unit | |
| | Stephen Gucker | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *30-58* is/are pending in the application.

4a) Of the above claim(s) *36-48 and 52-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-35,49-51 and 56-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

**1.** Applicant's election of Group I, claims 30-35 and 49-58, in the reply filed on 1/27/05 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). In addition, Applicant has elected the following species: a single agent binding growth hormone receptors: a) growth hormone or an analog thereof; a single agent effecting an increase in the active concentration of an agent which binds neural growth hormone receptors: b) GHRH; a single secondary neuroprotective agent: b) GPE; a single neuronal insult: stroke.

**2.** Claims 52-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 1/27/05.

**3.** The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**4.** Claims 30-35, 49-51, and 56-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for growth hormone (GH), does not reasonably provide enablement for an analog thereof, a functionally equivalent ligand, or a functionally equivalent endogenous ligand. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches GH but does not provide any working examples of the use of non-GH products that are neuroprotective. Furthermore, the claims are so broad as to encompass any product that possesses the *functionality* of GH without any limitation as to that product's *structure* or chemical composition as long as it possessed the biological properties of GH (*In re Fisher*, 166 USPQ 18). Because GH is a polypeptide, the structure or chemical composition of any product that would be encompassed by the mere functionality requirement of the instant claims is quite unpredictable, and to enable the full reasonable scope of the claims would require undue, painstaking experimentation (see Rudinger, page 6), even for those of highest skill in the art (i.e. physicians and scientists, again consult Rudinger). The instant disclosure does not provide sufficient working examples or guidance commensurate with the very broad scope of the claimed compositions and methods that would encompass unenvisioned functional embodiments of all manner of products, be they specifically undescribed endogenous polypeptides, synthetic GH-like polypeptides with additions, substitutions, or deletions to the GH amino acid sequence, carbohydrates, lipids, nucleic acids, smaller organic molecules, etc.

Likewise, claim 56 recites "a secondary neuroprotective agent" that is not IGF-1 when there is only one secondary neuroprotective agent present. "A secondary neuroprotective agent" is also only functionally defined, and is actually broader in scope than the GH analogs outlined above, and is not commensurate in scope with the supporting disclosure for the same reasons, because it is only defined by what it is *not* (i.e. not IGF-1), rather than being defined by what it *is*.

**5.** Claims 30-35, 49-51, and 56-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. No adequate description is given for the broad genus of GH analogs and neuroprotective agents because these analogs and agents are only functionally described, and the teachings of the specification do not reveal a generic underlying structure, composition, or motif by which the skilled artisan would recognize that the inventors had possession of the entire broad genus. Furthermore, the definition of "a secondary neuroprotective agent" is merely limited by the negative definition that it not be IGF-1, and not a positive recitation of what it actually is when the genus is infinitely large (even water is neuroprotective in the case of severe dehydration, etc.).

**6.** The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**7.** Claims 30-32 and 34-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Burman et al. ("Burman"). Burman discloses that growth hormone administered to the periphery of the human body has the inherent property of being able to pass into the cerebrospinal fluid of the human body (see Fig. 1-Fig. 2 and first paragraph of discussion on page 322), thereby coming into contact with the brain, and

by so doing inherently inducing a neuroprotective effect in a brain of a patient as recited by the instant claims (see *Ex parte Novitski*, 26 USPQ2d, 1389).

**8.** Claims 30-32 and 34-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Nyberg et al. ("Nyberg"). Nyberg teaches the administration of growth hormone to patients who are growth hormone deficient reduces their level of mental distress (pages 20-21) by improving their cognitive functions, energy, and emotions. Nyberg discloses that growth hormone administered to the periphery of the human body has the inherent property of being able to pass into the cerebrospinal fluid of the human body (see pages 20-21), thereby coming into contact with the brain, and by so doing inherently induces a neuroprotective effect in a brain of a patient as recited by the instant claims (see *Ex parte Novitski*, 26 USPQ2d, 1389).

**9.** Claims 30, 32-35, and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Golab et al. ("Golab") in light of Burman and/or Nyberg. Golab describes, beginning with the last paragraph on page 234, the treatment of stroke patients with STH (somatotropin or growth hormone) composition. The case studies on page 235 indicate that a 54 year-old woman who initially suffered paralysis of the extremities and face recovered functional movement for all but the left corner of her mouth after being administered growth hormone. The other case study indicates that a 58 year-old woman also recovered functional use of the right side of her body after being administered growth hormone. The first woman was diagnosed as having suffered a cerebral embolism and the second woman was diagnosed as suffering a cerebral hemorrhage and they were treated with growth hormone over a period lasting up to six or ten days.

The single reference Golab is being understood in terms of the undisclosed but inherent properties of growth hormone in light of the teachings of Burman and/or Nyberg that growth hormone administered to the periphery of the human body has the inherent property of being able to pass into the cerebrospinal fluid of the human body (see Fig. 1-Fig. 2 and first paragraph of discussion on page 322), thereby coming into contact with the brain, and by so doing induce a neuroprotective effect in a brain of a patient as recited by the instant claims and as observed in the recovery of the stroke patients administered growth hormone as described by Golab (see *Ex parte Novitski*, 26 USPQ2d, 1389).

The Examiner was unable to obtain an official written translation from the Polish for the Golab reference before a first office action on the merits for the case was due. A translation has been requested for the case file and will be forwarded to Applicant to review in a future office action in response to Applicant's response to this office action.

**10.** The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**11.** Claims 30-35, 49-51, and 58 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,187,906 B1 in view of Golab. The patented claims teach methods using GPE as a neuroprotective agent for dopaminergic neurons. The patented claims do not teach methods using GH as a neuroprotective agent. Golab does teach methods using GH as a neuroprotective agent in stroke as set forth in **¶9** above. It would have been obvious for one of ordinary skill in the art at the time of the invention to combine the two methods because each method is intended to produce the same result of neuroprotection and the ordinary artisan would find the suggestion *prima facie* obvious that a combination of two different methods intended to produce the same therapeutic result would be additive, thereby providing the motivation of neurologically improved patient care, as all neurons are subject to neuronal death from stroke, including dopaminergic neurons, and thus there is a reasonable expectation of success as demonstrated by the enabled patented claims.

**12.** The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned US 6,187,906 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was

made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Claim 50 is directed to an invention not patentably distinct from claims 1-11 of commonly assigned US 6,187,906 B1. Specifically, the patented claims teach methods using GPE as a neuroprotective agent.

**13.** The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**14.** Claims 30-35, 49-51, and 56-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Golab in view of Gluckman et al. (US 6,187,906 B1, "Gluckman").

Golab teaches methods using a GH composition as a neuroprotective agent in stroke as set forth in ¶9 above. Golab does not teach a GPE composition or methods of use. Gluckman (effective filing date August 11, 1997) does teach GPE compositions and methods of use (abstract, column 9, line 15 to column 10, line 5). It would have been obvious for one of ordinary skill in the art at the time of the invention to combine the two methods because each method is intended to produce the same result of neuroprotection for stroke (hypoxic-ischemic brain injury) and the ordinary artisan would find the suggestion *prima facie* obvious that a combination of two different methods intended to produce the same therapeutic result would be additive, thereby providing the motivation of neurologically improved patient care, as all neurons are subject to neuronal death from stroke, and there is a reasonable expectation of success as demonstrated by the enabled patented claims.

**15.** No claim is allowed.

**16.** Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technical Center 1600 general number which is (571) 272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (571) 272-0883. The examiner can normally be reached on Monday to Friday from 0930 to 1800. If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Janet Andres, can be reached at (571) 272-0867. The fax phone number for this Group is currently (571)-273-8300.

Stephen Gucker

June 27, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER